REMARKS

Claims 1 and 24 have been amended. Claims 1-22 and 24 are now pending in this application. Amendments have been made to clarify the claimed subject matter. Accordingly, the amendments do not constitute the addition of new matter. Applicant respectfully requests the entry of the amendments and reconsideration of the application in view of the amendments and the following remarks.

Specification

The Examiner objects to the specification as containing an embedded hyperlink at page 14, line 29. Applicants have deleted the hyperlink. This objection may be withdrawn.

Double patenting

Claims 1-22 and 24 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 41-64 of copending Application No. 09/859,651.

Claims 1-22 and 24 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of copending allowed Application No. 09/929,945.

The above grounds of rejection are obviated by Applicants' terminal disclaimer filed herewith.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-22 and 24 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which is not described in the specification in such a way so as to enable one skilled in the art to which it pertains to make and/or use the invention.

The Examiner draws attention to the phrase "cultivating the *E. coli* host cell under a culture condition that induces lytic growth of said cell without lysis until a desired level of production of said protein is reached, wherein said protein is produced as a soluble biologically-active protein." (claim 1). The Examiner states that producing soluble, biologically active protein in *E. coli* is unpredictable and that the presence or absence of working examples becomes relevant to enablement of the invention. The Examiner asserts that none of the working examples teach cultivation of a host cell under a culture condition that induces lytic growth. In response, Applicants have amended claim 1 to remove the word "lytic". Applicants would like to clarify that the cells are infected with the bacteriophage but it is not necessary to induce the

cells to lyse. The cells will eventually lyse but, by delaying lysis, the recombinant *E. coli* are able to produce soluble, biologically active protein in good yield.

The Examiner also states that the specification does not teach how to determine whether or not "a desired level of production of said protein is reached" and does not teach how to control the timing of lysis until after that point. It is respectfully submitted that one skilled in the art would know how to apply the claimed method to proteins in general based upon the teachings of the present specification. The present specification exemplifies the presently claimed invention for 3 different human proteins and one bacterial protein including 4 forms of human FGF. Thus, 7 different proteins are exemplified. The method is reproducible for all of these diverse proteins. The biological activity of the FGF 155 produced in Example 1 is demonstrated in Example 6. The biological activity of the human Growth Hormone is described in the specification at page 23, lines 12-14. The biological activity of the interferon α-2b produced according to the specification is described at page 24, lines 12-19. In all cases, the specification teaches release into the supernatant. Thus, the specification teaches the production of soluble, biologically-active proteins as claimed.

While the specification teaches that the cells were cultivated for 14 hours after infection with the phage, one skilled in the art would know how to assay for the protein of interest and adjust the cultivation period to produce the optimum protein for their particular requirements. However, in order to address the Examiner's concerns, the phrase "until a desired level of production of said protein is reached" has been deleted from claim 1.

The Examiner also asserts that the specification does not teach how to control the timing of lysis until the desired level of protein production is reached. In response, it is not necessary to induce lysis as clarified above. In practice, lysis is delayed to produce as much protein as possible. Applicants submit that the present claims are fully enabled by the teachings of the present specification.

Regarding claim 24, the Examiner states that the working examples again do not teach lysis of the producer cells and do not teach the concentration of the protein in the culture medium. In response, claim 24 has been amended to clarify that the *E. coli* cells are cultivated under a culture condition that delays lysis. The recitation that the concentration is greater than 100 μg/ml has been deleted.

In view of Applicants' amendments and arguments, reconsideration and withdrawal of this ground of rejection is respectfully requested.

Prior art

The Examiner's indication that the claims are free of the art is gratefully acknowledged.

CONCLUSION

In view of Applicants' amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: Oct. 21, 2003

By: Che S. Chereskin

Che Swyden Chereskin, Ph.D.
Registration No. 41,466
Agent of Record
Customer No. 20,995
(949) 760-0404

H:\DOCS\CSC\PHAGE\006A\PHAGE006A_AMD.DOC
092403